REMARKS

Entry of the foregoing amendment is requested.

The title has been amended, the status (and relationship) of the priority documents is updated, and page 16, line 15 is corrected.

Should the Examiner have specific complaints, rather than the generic one at point 7 of the action, he should so state them.

The Examiner grants priority to 09/418,568 filed October 18, 1999.

This is not correct. Please see Serial No. 09/354,243, filed July 16, 1999. **Priority is claimed in this application**. SEQ ID NOS.: 24 and 25 are set forth in 09/354,243 application. For the Examiner's convenience, a copy of U.S. Patent No. 6,359,117 is attached hereto.

The Examiner is called upon to correct his statements regarding the priority claim. applicants will proceed under the assumption that priority to July 16, 1999 will be granted.

If it is not, applicants will petition the denial.

With respect to the Examiner's statements inviting applicants to confirm that IL-TIF/IL-21 has been renamed IL-22, the inventors did not do so. Rather, the relevant administrative authorities have. Please see the attached copy of a page from http://www.gene.ucl.ac.uk/cgi-bin/nomenclature/get_data.pl?hgnc_id=14900. Please note the Aliases.

The Examiner has then rejected all of the pending claims under 35 U.S.C. § 112, first paragraph, as allegedly being non-enabled. The Examiner's argument is set forth at point 9, and contains both accurate, and inaccurate information. Further, the Examiner's argument is diffuse and non-conclusory, making it impossible to determine if and when a point is made.

The passage beginning "The instant claims are drawn broadly" is correct; however, the following paragraph ("Applicant has not disclosed...") is not.

The specification, via its description of properties, sequences, and hybridization conditions, does disclose more than the specific sequences set forth in the sequence listings. Assuming arguendo, however, that even if only these sequences were shown there is no rule, regulation or statute that would limit applicants to specific sequences. In fact, the law is the

contrary: patent specifications are presumed to be enabled, regardless of the degree or amount of disclosure. The burden lies with the Examiner to prove that the specification is NOT enabled, i.e., that one could not obtain other materials sharing the properties of the claimed invention, without undue experimentation.

That is the law. With that in mind, one turns to the Examiner's evidence, or in this case, the lack thereof.

According to the Examiner:

> "Applicant disclosed the structural basis or nexus for activation of STAT 3 by the T cell derived inducible factor (TIF) encoded by the disclosed nucleic acid consisting of cDNA and genomic sequences of TIF.
>
> Applicant has not provided sufficient biochemical information (e.g., molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies any mammalian T cell inducible factor. T cell inducible factor may have some notion of the function of the protein, however, there is insufficient guidance and direction as how to make and use the claimed genus of T cell inducible factors, commensurate in scope with the claimed invention."

First of all, applicants do not have to supply a structural basis for the activation of STAT 3. There is no such law requiring this. Further, contrary to the Examiner's position, applicants have provided a molecular weight range. The specification does teach amino acid sequences. Protocols are given in careful detail which show how the molecules were obtained. It is the Examiner's burden to show that one could not obtain additional materials. He has not done so.

The Examiner then goes on to say:

> "For example, the specification discloses a diversity of structure and function of the disclosed T cell inducible factors encoded by nucleic acid molecules consisting of SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 24 and SEQ ID NO: 25."

The point regarding diversity of structure is not understood. Further, the Examiner omits the fact that shared function is shown, i.e., the ability to activate STAT 3.

Further, the Examiner misstates the specification. Examples 12-14 do not show what the Examiner says they do. Even if they did, how is this relevant? The issue is: do the

molecules stimulate STAT 3? Where is the Examiner's evidence that they do not?

The Examiner then turns to his "structural nexus" argument again:

> "Although the instant specification discloses high homology between mouse TIF alpha and beta (and therefore hybridizes to mouse TIF alpha under stringent conditions), there is insufficient guidance and direction as to critical common structural elements that define a T cell inducible factor or that define a T cell inducible factor alpha or beta and, in turn, the nexus between structure in an T cell inducible factor and its ability to stimulate the expression of STAT 3."

Again, applicants call upon the Examiner to show support in the law for this requirement.

The statement which follows:

> "T cell inducible factors, including those encoded by SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 24, and SEQ ID NO: 25., which stimulate STAT 3, that is, they are not related as a ligand-receptor binding pair."

is incomprehensible. What is the Examiner's point?

The Examiner then goes on to cite non-prior art work by the inventors. The point behind this discussion is obscure. Even if everything the Examiner said were true - and applicants do not agree that it is - why does the Examiner ignore the common property of STAT 3 activation? The fact that all TIF molecules do not induce STAT 3 in all cells is absolutely irrelevant. The law states quite clearly that 100% functionality is never required.

The Examiner then makes the following statement:

> "It is noted that the starting material of peripheral blood cells for human TIF was stimulated with anti-CD3 antibodies and not IL-9 (see page 23, paragraph 1 of the instant specification). Anti-CD3 antibodies can stimulate a variety of molecules and are not limited to stimulating TIF alpha or beta. The instant specification further discloses that TIF mRNA can be expressed in the absence of IL-9 (see Example 14, particularly page 17, lines 7-8 of the instant specification).
>
> In addition, it is noted that the "T cell inducible factor" has been renamed "IL-TIF/IL-21", which, in turn, has been renamed "IL-22" by the coinventors (see page 1, column 1, Background and Prior Art of Renauld et al., US 2003/0012788 A1). Here, it is

> noted that the conventors have shown that the signaling pathways associated with IL-22 were not the same as IL-10, as previously thought (see entire document, including page 1, column 2, paragraph 2).
>
> Furthermore, Ebert (Trends in Immunology 23:341-342, 2002) notes confusion and ambiguities in labeling cytokines as interleukins, including IL-TIF/IL-21 described by the instant invention Dumoutier."

The reasons for this statement are absolutely unclear. Why does the remaining of molecules have to do with this?

With respect to the citation to non-prior art Skolnick, Applicants did not assign functional activities based on sequence homology: they did the experiments. The claimed molecules did activate STAT 3.

The Examiner's entire argument beginning on the unnumbered page that begins "Applicant is relying," is conclusory and has no support in the art.

Further, the art supports applicants conclusions. The Examiner has made the Ebner application of record. Peprotech is selling products referred to as IL-22. Please see the attached. Hence, applicants' assertions are borne out by others. The Examiner's argument cannot be maintained. Not only has the Examiner not provided any support for his position, the fact is that other molecules are known which satisfy the claims. As such, the rejection should be withdrawn.

The Examiner has rejected all claims under 35 U.S.C. § 102(e) in view of Ebner, US 2003/003545 A2. Ebner has an effective prior art date of May 27, 1999. applicants reduced their invention to practice before this. Please see the attached Declaration of the inventors, with supporting data from their laboratory notebooks.

The Examiner makes the following statement at the end of the Office Action:

> "It is noted that when the claims of the reference U.S. Patent or U.S. Patent application publication and the application are directed to the same invention or are obvious variants, an affidavit or declaration under 37 C.F.R. § 1.131 is not an acceptable method of overcoming the rejection."

It is noted that the Examiner does not rely on the claims of Ebner, nor does the Examiner set forth a rejection under 35 U.S.C. § 102(g). This is the proper approach if the

Examiner believes that the same invention is being claimed.

The Examiner also cites to MPEP 2308.01; however, this section of the MPEP deals with issued patents and applications, not two applications. As the Examiner has not premised any rejection on the claims of Ebner, the rejection can be overcome by showing prior reduction to practice, which applicants have done.

All issues appear to have been addressed and overcome. Allowance of this application is believed proper, and is urged.

Respectfully submitted,

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Attachments:
Copy of web page
U.S. Patent No. 6,359,117
Peptrotech
Declaration w/ notebook papers

~~ISOLATED NUCLEIC ACID MOLECULES WHICH ENCODE T CELL INDUCIBLE FACTORS (TIFs), THE PROTEINS ENCODED, AND USES THEREOF~~

ISOLATED NUCLEIC ACID MOLECULES ENCODING T CELL DERIVED INDUCIBLE FACTORS

PAGE 1, LINES 2-4, REPLACE WITH

~~This application is a continuation in part of Serial No. 09/354,243, filed on July 16, 1999, which in turn is a continuation in part of Serial No. 09/178,973, filed October 26, 1998. Both of these applications are incorporated by reference in its entirety.~~

This application is a continuation of Serial No. 09/419,568 filed October 18, 1999, now U.S. Patent No. 6,331,613, which is a continuation-in-part of Serial No. 09/354,243, filed on July 16, 1999, now U.S. Patent No. 6,359,117, which in turn is a continuation-in-part of Serial No. 09/178,973, filed on October 26, 1998, now U.S. Patent No. 6,274,710. All of these applications are incorporated by reference in their entirety.

mut6, has a mutation which renders the receptor unable to activate STAT5, while retaining the ability to activate STAT1 and STAT3. Finally, cell line BW-mut7 has a single mutation which renders the IL-9 receptor unable to activate STAT1 and STAT3, but which retains the ability to activate STAT5.

Cell stimulation, isolation of total RNA, reverse transcription and amplification of cDNA were all carried out as described in example 10 (Cells were stimulated for 24 hours. Both human and murine recombinant IL-9 were used). The PCR products were analyzed on an ethidium bromide stained, 1% agarose gel, as describe supra.

The analysis revealed that human IL-9 did not induce expression in BW-Phe116, suggesting that STAT transcription factors are implicated. It was found that IL-9 induced TIF expression in the BW-mut6 mutant, but not the mut7 variant, suggesting that STAT1 or STAT3 are involved, but not STAT5.

Example 13

The expression of TIF mRNA in normal mouse spleen cells was then studied.

Spleen cells from 10–12 week old ~~Balb/c~~ BALB/c mice were cultured for 24 hours in control medium or the control medium supplemented with 20μg/ml of LPS (which activates B lymphocytes and macrophages), or ConA (which activates T cells), or ConA plus 1% of a blocking antiserum against murine IL-9, with β actin being used as a control. Purification of RNA, RT-PCR analysis were carried out as described supra.